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(54) Title: TASTE-MASKED ACETAMINOPHEN SUSPENSIONS AND METHODS OF MAKING THE SAME

(57) Abstract

Acetaminophen composition in which the taste of the acetaminophen is effectively masked by suspending the drug in a suspension medium containing suspension agent and additive agents that decrease the solubility of the acetaminophen in aqueous solution. The additive agents preferably include sweetening agents. The concentration of the sweetening agent is preferably at least about 25 weight percent of the acetaminophen composition.

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TASTE-MASKED ACETAMINOPHEN SUSPENSIONS AND METHODS OF MAKING THE SAME

Field of the Invention

The present invention relates to acetaminophen compositions in which the acetaminophen is presented in taste-masked form. More particularly, the present invention relates to an acetaminophen composition wherein the acetaminophen solubility is limited by the presence of additive agents, such as sweetening agents.

Background of the Invention

Acetaminophen is a widely used over-the-counter drug which has beneficial pain relieving and fever relieving properties. Acetaminophen is commonly taken as a tablet by the vast portion of the population. However, the tablet form is hard to administer in treating the elderly and the young. Therefore, liquid formulations of acetaminophen are commonly administered for these patients. However, in liquid form such as in an elixir formulation, the acetaminophen is dissolved into solution. Once dissolved, the strongly unpalatable taste of acetaminophen is found to be objectionable. Therefore, noncompliance among liquid acetaminophen patients is

commonplace.

Various techniques have been used to mask the taste of acetaminophen in non-liquid forms such as tablet coatings or spray dried particles such as are described in U.S. Patent No. 4,760,094. Cooper, U.S. Pat. No. 4,794,112, suggests the use of sweetening agents and suspending agents for oral administration of an acetaminophen and hydroxyzine composition, however it is not shown how to prevent the acetaminophen from substantially dissolving in solution. Therefore, a need exists for a liquid acetaminophen composition which is suitable for oral administration in which the acetaminophen is effectively presented in a taste-masked form.

Summary of the Invention

The invention provides an acetaminophen composition in taste-masked form, suitable for oral administration, containing acetaminophen in an aqueous medium. The acetaminophen composition contains acetaminophen in an amount of up to about 10% by weight, preferably from about 2 to about 8% by weight, in an aqueous medium. The aqueous medium contains suspension agent for dispersing the acetaminophen and additive agent for decreasing the solubility of the acetaminophen in the aqueous medium to below 1.3% wt. The additive agent is preferably comprised of sweetening agents which are preferably present in an amount of at least about 25% by weight of the acetaminophen composition.

Various preferred embodiments of the invention can be prepared. The suspension agent is preferably present in an

amount of from about 0.03 to about 0.3% by weight and a preservative agent is also preferred to be present in the composition. The sweetening agent preferably comprises at least one agent selected from the group consisting of sucrose, glucose, fructose, lactose, maltose, sorbitol, mannitol, and maltitol, and can consist of mixtures of these.

Detailed Description of the Preferred Embodiments

The acetaminophen composition of the present invention is characterized by having a palatable taste and with only a slight gritty feel. The composition is a liquid formulation in which the acetaminophen is suspended, and slightly dissolved, in an aqueous medium containing a suspension agent for dispersing the acetaminophen and an additive agent that decreases the solubility of the acetaminophen in the aqueous solution. The additive agent is preferably a sweetening agent. It has been surprisingly found that when the concentration of additive agent and suspension agent are properly adjusted, the taste of the acetaminophen can be masked effectively.

The acetaminophen which is useful in the present invention is particulate acetaminophen of pharmaceutical grade. It is preferred to use acetaminophen with a small average particle size to decrease the gritty feel of the drug. Generally the particle size of the acetaminophen is such that about 99% wt. is below about 420 microns and about 97% wt. is below about 250 microns. In a preferred embodiment, about 90% wt. is below about 150 microns and about 35% wt. is below about 40 microns, such acetaminophen is commercially available as

acetaminophen Powder grade from Mallinckrodt, Inc., St. Louis, Mo. A more preferred embodiment contains acetaminophen having about 70% wt. below about 40 microns such as the Fine Powder grade available from Mallinckrodt, Inc. In certain applications, a very fine acetaminophen is preferred having about 90% wt. below about 40 microns such as the Micronized acetaminophen from Mallinckrodt, Inc.

As known by those skilled in the art, the acetaminophen is administered in dosages that effect the desired therapeutic result, "therapeutically effective amount", and the acetaminophen is generally present in the inventive compositions up to about 10% by weight, preferably from about 2 to about 8% by weight, and most preferably from 2 to 5% by weight of the final composition. Common dosage forms are in 5-10 ml quantities.

The acetaminophen compositions of the present invention contain a suspension agent or mixtures of suspension agents. Suitable suspension agents are well known in the art and include, but are not limited to, xanthan gum, sodium alginate, carrageenan, carboxylmethylcellulose, algin, guar gum, propylene glycol alginate, and mixtures thereof; xanthan gum being preferred. The suspension agent is useful to keep the particulate acetaminophen concentration uniform in the composition. The suspension agent is preferably present in an amount of from about 0.03 to about 0.3% by weight of the composition, more preferably about 0.05 to about 0.2% by weight. The weight ratio of acetaminophen to suspension agent is typically about 1:0.01 to about 1:0.08.

The suspension agent is preferably accompanied by a dispersant. The dispersant acts to aid in making the aqueous solution containing the suspension agent homogeneous. If the dispersant is not employed, vigorous agitation is usually necessary to suspend the suspension agent in the aqueous medium. Dispersants which can be used in the present invention are well known and include, for example, glycerin, propylene glycol, ethanol and combinations thereof. Typically, the dispersant is present from about 0.15 to about 0.5% by weight of the composition.

The additive agent is present in the composition in a relatively high concentration. The high concentration of additive agent acts to limit the solubility of the acetaminophen in the liquid composition. The unpalatable taste of the liquid acetaminophen composition is thereby reduced due to the decreased solubility of the acetaminophen. The amount of solubilized acetaminophen in the compositions of this invention is generally below 1.3% by weight, preferably below 1.1% by weight, more preferably below 0.95% by weight, and most preferably below 0.85% by weight.

The additive agent is preferably comprised of a sweetening agent or mixtures of sweetening agents so that not only is the bitter taste of the acetaminophen in solution limited, but it is replaced by the pleasant tasting sweetener. Other agents, besides sweetening agents, can also be used to limit the solubility of the acetaminophen. These agents include such compounds as salts or polyol compounds such as propylene glycol and polyethylene glycol. These agents are

preferably taste-neutral, and the amount of these agents is preferably limited so that they do not significantly alter the taste of the final composition as being unpalatable. Preferably, the additive agent is at least 75% wt., more preferably at least 90% wt., and most preferably 100% wt. sweetening agent.

Sweetening agents which can be used in the present invention to limit the solubility of the acetaminophen in aqueous solution are those of the polyol type, particularly those which are highly soluble in water. Sweetening agents of this type include the sugars such as sucrose ($C_{12}H_{22}O_{11}$), glucose ($C_6H_{12}O_6$), fructose ($C_6H_{12}O_6$), lactose ($C_{12}H_{22}O_{11}$), and maltose ($C_{12}H_{22}O_{11}$), preferably in pharmaceutical grades. Natural and semi-refined sweetening agents such as honey and corn syrups, which are mixtures of sugars with other related compounds, can be used, as well as polymers of sugars such as maltodextrins. Low levels of artificial sweetners such as aspartame and saccharin can also be used.

The sweetening agent can also include polyhydric alcohols such as sorbitol ($C_6H_{14}O_6$), mannitol ($C_6H_{14}O_6$), and maltitol ($C_6H_{11}O_5[C_6H_{10}O_5]_nC_6H_{13}O_6$), n=1-20, - otherwise known as hydrogenated glucose and hydrogenated starch hydrolysate, preferably in pharmaceutical grades. The sweetening agent can also be a mixture of any of the above-mentioned compounds.

The additive agent concentration is at least 25% wt., preferably at least 50% wt., more preferably at least 55% wt., and in some cases at least 60% wt., of the acetaminophen composition. The amount of additive agent will generally not

exceed about 85% wt. of the composition, and is limited by its solubility. The drug to additive agent weight ratio is generally about 1:5 to about 1:40, preferably about 1:10 to about 1:30.

Various flavors such as mint, cherry, punch, spearmint, grape and the like can also be added to the composition. If present, such flavoring agents are preferably provided in an amount of up to about 0.2% wt. of the composition. The amount of flavoring agent is limited by taste considerations at higher concentrations.

The acetaminophen composition can also contain preservatives. The preservatives which can be used are well known in the art as common food preservatives. Examples are set forth in the CTFA Cosmetic Ingredient Handbook, published by Cosmetic, Toiletry, and Fragrance Assoc., Wash. D.C. (1988), which is incorporated herein in its entirety. Preferred preservatives include methylparaben, sodium benzoate, isopropylparaben, sorbic acid and mixtures thereof, preferably sodium benzoate. Antioxidants, such as BHT, can also be used.

The pH of the acetaminophen composition is held below about 6, and most preferably between about 3.5 and 5. The pH is preferably maintained at these levels to sustain a long shelf life since the preservatives usually do not work well in a high pH system. Any appropriate ingestible acid may be used to modify the pH of the acetaminophen composition, including hydrochloric, citric, and acetic acid.

The final density of the acetaminophen composition generally ranges from about 1.1 to about 1.35 g/ml, preferably

about 1.25 to about 1.32 g/ml. The viscosity of the acetaminophen composition generally ranges from about 200-900 centipoise, preferably from about 300-700 centipoise.

Preferred compositions of the present invention contain 2-5% wt., preferably 2-3% wt. acetaminophen; 30-40% wt., preferably 33-37% water; 0.15-0.2% wt. dispersant; 0.03-0.1% wt., preferably 0.05-0.1% wt. suspension agent; and 55-65% wt. sweetener. The composition can also contain 0.05-0.1% wt. preservative.

The acetaminophen compositions of the present invention can be prepared by providing particulate acetaminophen and admixing it into an aqueous solution containing the suspension agent and the additive agent, the pH of the aqueous solution having been adjusted using an ingestible acid. The aqueous solution can also contain preservatives, dispersants, and flavoring agents.

The acetaminophen compositions of the present invention can also be prepared by first preparing a suspension agent solution containing the suspension agent in an aqueous medium. It is preferred that the aqueous solution contain about 1 to about 5, most preferably about 2 weight percent suspension agent. The suspension agent solution can also contain dispersant and preservative. The particulate acetaminophen is then mixed into the suspension agent solution. An aqueous solution containing the additive agent is then added to the mixture; this solution typically contains a preservative.

The invention is further illustrated by the following

non-limiting examples.

Example 1

An acetaminophen composition was produced which effectively masked the taste of the acetaminophen. A 3.2 g sample of acetaminophen was placed in a container. To this was added 5 g of an aqueous polymer solution containing 2 wt.% xanthan gum, 6 wt.% glycerin, and 0.2 wt.% methylparaben. The drug and polymer solution was mixed and rubbed thoroughly with a pestle.

119.9 g of a sweetening solution containing 65 wt.% sucrose, 0.08% wt. sodium benzoate with a pH adjusted to 4.3 using hydrochloric acid was incrementally added to the drug/polymer mixture. Pestle rubbing was continued throughout the addition. Finally, 0.2 g of fruit punch flavor was added to the suspension.

The acetaminophen composition obtained was a viscous suspension with a pH=4.3, containing 160 mg of acetaminophen in about 5 ml of the composition. The final composition had a suspension agent concentration of 0.08% wt., and a sweetening agent concentration of 61% wt.

Example 2

An acetaminophen composition was produced which effectively masked the taste of the acetaminophen. A 6.5 g sample of acetaminophen was placed in a container. To this was added 10 g of the polymer solution of Example 1. The drug and polymer solution was mixed and rubbed thoroughly with a pestle.

109 g of a sweetening solution containing 65 wt.% sucrose, 0.08% wt. sodium benzoate with a pH adjusted to 4.3

using acetic acid was incrementally added to the drug/polymer mixture. Pestle rubbing was continued throughout the addition. Finally, 45 mg of mint flavor was added to the suspension.

The acetaminophen composition obtained was a viscous suspension with a pH=4.4, containing 325 mg of acetaminophen in about 5 ml of the composition. The final composition had a suspension agent concentration of 0.16% wt., and a sweetening agent concentration of 56.5% wt.

Example 3

An acetaminophen composition was prepared containing 5.1% wt. acetaminophen, 0.08% wt. xanthan gum, and about 60% wt. sucrose. The composition was prepared by adding 1.5 g of the polymer solution of Example 1 to 1.95 g acetaminophen. The mixture was thoroughly mixed in a ceramic vessel until the drug was wetted and dispersed homogeneously. Next, 34.7 g of an aqueous syrup (65% wt. sucrose, 0.08% wt. sodium benzoate) having a pH adjusted to 4.2 with HCl was incrementally admixed to the vessel. The final mixture had a volume of 30 ml.

Example 4

An acetaminophen composition was prepared containing 5.1% wt. acetaminophen, 0.05% wt. xanthan gum, 0.3% wt. sodium carboxymethylcellulose and about 57% wt. sucrose. The composition was prepared by adding 0.9 g of the xanthan gum solution of Example 3 to 1.95 g acetaminophen. Additionally, 1.5 g of an 8% wt. aqueous solution of sodium carboxymethyl cellulose was added. The mixture was thoroughly mixed in a ceramic vessel until the drug was wetted and dispersed homogeneously. Next, 33.5 g of the aqueous syrup of Example 3

was incrementally admixed to the vessel. The final mixture had a volume of 30 ml.

Example 5

An acetaminophen composition was prepared containing 5.1% wt. acetaminophen, 0.05% wt. xanthan gum, and about 60% wt. sucrose. The composition was prepared by adding 0.9 g of the 2% wt. xanthan gum solution of Example 3 to 1.95 g acetaminophen. The mixture was thoroughly mixed in a ceramic vessel until the drug was wetted and dispersed homogeneously. Next, 35.4 g of the aqueous syrup of Example 3 was incrementally admixed to the vessel. The final mixture had a volume of 30 ml.

Example 6

An acetaminophen composition was prepared containing 5.1% wt. acetaminophen, 0.16% wt. xanthan gum, and about 56% wt. sucrose. In a stainless steel bowl, 65 g acetaminophen and 100 g of the xanthan gum solution of Example 3 were added and mixed to form a homogeneous mixture. To this was added 1090 g of the syrup of Example 3. The final mixture had a volume of 1000 ml.

Example 7

An acetaminophen composition was prepared containing 2.5% wt. acetaminophen, 0.16% wt. algin, and about 58% wt. sucrose. The composition was prepared by adding 3 g of a 2% wt. aqueous algin solution to 0.96 g acetaminophen. The mixture was thoroughly mixed in a ceramic vessel until the drug was wetted and dispersed homogeneously. Next 34 g of the syrup of Example 3 was incrementally admixed to the vessel. The final mixture had a volume of 30 ml.

Example 8

An acetaminophen composition was prepared containing 2.5% wt. acetaminophen, 0.08% wt. guar gum, and about 58% wt. sucrose. The composition was prepared by adding 3 g of a 1% wt. aqueous guar gum solution to 0.96 g acetaminophen. The mixture was thoroughly mixed in a ceramic vessel until the drug was wetted and dispersed homogensouly. Next 34 g of the syrup of Example 3 was incrementally admixed to the vessel. The final mixture had a volume of 30 ml.

Example 9

An acetaminophen composition was prepared containing 2.5% wt. acetaminophen, 0.16% wt. propylene glycol alginate, and about 58% wt. sucrose. The composition was prepared by adding 3 g of a 0.2% wt. aqueous propylene glycol alginate to 0.96 g acetaminophen. The mixture was thoroughly mixed in a ceramic vessel until the drug was wetted and dispersed homogeneously. Next 34 g of the syrup of Example 3 was incrementally added to the vessel. The final mixture had a volume of 30 ml.

Example 10

A suspension of 2.5% w/v acetaminophen was prepared using sucrose and sorbitol as sweetening agents. 15 g of the aqueous polymer solution of Example 3 (2% Xanthan gum solution), 121.4 g of a 70% wt. sorbitol solution (pH adjusted to 4.2 with HCl preserved with sodium benzoate), and 493.8 g of the sucrose sweetening solution of Example 3 were mixed in a 1 liter beaker until a homogeneous solution was obtained. Stirring was continued and 16 g of acetaminophen was added to the solution. Stirring was continued for 15 minutes. 500 ml (646.2 g) of the final composition was produced.

Example 11

A suspension of 2.5% wt. acetaminophen was prepared using sucrose and sorbitol as sweetening agents. 15 g of the aqueous polymer solution of Example 3 (2% Xanthan gum solution), 242.9 g of a 70% wt. sorbitol solution (pH adjusted to 4.2 with HCl preserved with sodium benzoate), and 370.3 g of the sucrose sweetening solution of Example 3 were mixed in a 1 liter beaker until a homogeneous solution was obtained. Stirring was continued and 16 g of acetaminophen was added to the solution. Stirring was continued for 15 minutes. 500 ml (644.2 g) of the final composition was produced.

Example 12

Suspensions of 2.5% wt. acetaminophen containing various amounts of water and sucrose were made by mixing in a mortar and pestle. In each sample, 0.96 g acetaminophen was weighed and added to the mortar, 1.5 g of polymer solution (2% wt. xanthan gum, 6% wt. glycerine, 0.2% wt. methyl paraben) was

added, and then mixed and rubbed thoroughly with a pestle. In the case of Sample 1, 36.00 g of syrup (65% wt. sucrose, 0.08% wt. Na benzoate, with pH adjusted to 4.2 +/- 0.1 using hydrochloride acid) was added in increments to the polymer/drug admixture with mixing and rubbing action in between the additions. In the case of Sample 2, 32.00 g of pH adjusted syrup was added in the manner described for Sample 1, then 3.00 g of 0.1% Na benzoate in water, pH = 4.2 +/- 0.1 was added in increments to the polymer/syrup/drug mixture, with mixing action in between the increments. Samples 3, 4 and 5 were prepared in the same way, except the amounts of low pH syrup added were 28.13 g, 18.46 g, and 9.23 g, respectively; and the amounts of low pH water added were 6.00 g, 13.40 g, and 20.47 g, respectively. Sample 6 was also prepared in this manner, but no syrup was added; 27.5 g low pH water was added to the polymer/drug mixture directly, in increments, with mixing action in between the increments. Suspensions were tasted for bitterness level at this point.

Each suspension was then centrifuged for 20 minutes at 7000 rpm to sediment the drug in particulate form. Supernatents were decanted and filtered through a 5.0 μm filter. The concentration of acetaminophen in the supernatants was analyzed by USP HPLC method.

The results of the HPLC assay are shown in the Table and indicate that the concentration of acetaminophen in solubilized form is decreased when the water in the suspension is replaced by the sucrose.

Table

SAMPLE	1	2	3	4	5	6
Water concentration (wt%)	36	41	47	62	78	97
Sucrose concentration (wt%)	61	56	50	35	19	0
Acetaminophen concentration (wt%)	0.78	0.86	0.93	1.07	1.26	1.42

Example 13

A 2380 kg (490 gallon) batch of the acetaminophen suspension of the present invention was prepared. To a cleaned sanitized stainless steel vessel was added 222.5 gallons of USP water and heated to 115°F. 4.17 kg of glycerin was added and mixed thoroughly for about 30 minutes. Xanthan Gum, 1111 g (Keltrol T) was slowly added with mixing continued for 30 minutes. The temperature was maintained and the mixing was continued and 1019 g artificial cherry flavor was added over a 15 minute period followed by the addition of 1470 kg sucrose and 1854 g USP sodium benzoate over a 25 minute period. The temperature was then lowered to 75°F. 450 g hydrochloric acid (37%) was admixed (15 min.) and the pH of the mixture was found to be about 4.5. To this was admixed 224 g FD&C Red dye #40 and stirring was continued for about 2.5 hours. 59.31 kg of USP micronized acetaminophen from Mallinckrodt, Inc. was admixed with continued stirring over a period of 1 hour. The mixture was passed through a 20 mesh screen into 50 gallon drums. The final composition had about 2.5 wt.% acetaminophen, 62 wt.% sucrose, 0.05 wt.% xanthan gum, 0.2 wt.% glycerin, 35 wt.% water, 0.08 wt.% sodium benzoate, 0.02 wt.% HCl (37%), 0.04 wt.% cherry flavor, and 0.01 wt.% coloring.

Example 14

A 2380 kg (490 gallon) batch of the acetaminophen suspension of the present invention was prepared. To a cleaned sanitized stainless vessel was added 222.5 gallons of USP water and heated to 115°F. 4.17 Kg of glycerin was added and mixed with constant stirring for 35 minutes. Xanthan Gum (1.111 Kg) was slowly educted with mixing for 30 minutes. While maintaining a temperature of 115°F and mixing to create a vortex, sucrose (1,470 Kg) was added over a 25 minute period. Mixing was maintained and the mixture was cooled to 75°F. 450g of 37% HCl was added slowly with mixing continued for 15 minutes. The pH of a sample was measured to be 4.5. 224g of Red Dye #40 was added with stirring continued for 2.5 hours. Mallinckrodt acetaminophen USP fine powder (59.31 kg) was added over a period of 1 hour. Mixing was maintained for 90 minutes.

Artificial cherry flavor 750g was added with stirring for 60 minutes. The mixture was transferred through a 20 mesh screen into 50 gallon drums.

What is claimed is:

1. An acetaminophen composition in taste-masked form, suitable for oral administration, comprising up to about 10% wt. acetaminophen in an aqueous medium comprising (i) suspension agent, and (ii) sweetening agent, for decreasing the solubility of the acetaminophen in the aqueous medium, in an amount of at least 25% by weight of said composition.

2. The acetaminophen composition of claim 1 wherein the acetaminophen concentration is from about 2 to about 8% wt. of the composition.

3. The acetaminophen composition of claim 2 wherein the sweetening agent comprises at least one sweetening agent selected from the group consisting of sucrose, glucose, fructose, lactose, maltose, sorbitol, mannitol, and maltitol.

4. The acetaminophen composition of claim 2 wherein the sweetening agent is present in an amount of at least 50 weight percent of the composition.

5. The acetaminophen composition of claim 4 wherein the sweetening agent is present in an amount of at least 55 weight percent of the composition.

6. The acetaminophen composition of claim 2 wherein the solubilized acetaminophen in the composition is below 1.10% wt.

7. The acetaminophen composition of claim 2 wherein the solubilized acetaminophen in the composition is below 0.95% wt.

8. The acetaminophen composition of claim 2 wherein the solubilized acetaminophen in the composition is below 0.85% wt.

9. The acetaminophen composition of claim 4 wherein the suspension agent is present in an amount of from about 0.03 to about 0.3% by weight of the composition.

10. The acetaminophen composition of claim 4 wherein the suspension agent is selected from the group consisting of xanthan gum, sodium alginate, carrageenan, carboxylmethylcellulose, algin, guar gum, propylene glycol alginate, and mixtures thereof.

11. The acetaminophen composition of claim 4 further comprising a preservative selected from the group consisting of methylparaben, isopropylparaben, sodium benzoate, sorbic acid and mixtures thereof.

12. The acetaminophen composition of claim 4 further comprising dispersant to aid in the dispersion of the suspension agent in the aqueous medium.

13. The acetaminophen composition of claim 12 wherein the dispersant is selected from the group consisting of glycerin and propylene glycol and mixtures thereof.

14. An taste-masked acetaminophen composition suitable for oral administration, comprising from about 2 to about 8% by weight acetaminophen in an aqueous medium comprising (i) suspension agent, and (ii) additive agent for decreasing the solubility of the acetaminophen in the aqueous medium to below 1.3% wt., wherein the additive agent is present in an amount of at least 25% by weight of the composition.

15. The acetaminophen composition of claim 14 wherein the additive agent comprises sweetening agent in an amount of at least 50% by weight of said composition.

16. The acetaminophen composition of claim 15 wherein the sweetening agent comprises at least one sweetening agent selected from the group consisting of sucrose, glucose, fructose, lactose, maltose, sorbitol, mannitol, and maltitol.

17. The acetaminophen composition of claim 16 wherein the additive agent further comprises at least one additive selected from the group consisting of propylene glycol and polyethylene glycol.

18. The acetaminophen composition of claim 16 wherein the amount of solubilized acetaminophen is below 1.1% wt.

19. The acetaminophen composition of claim 18 wherein the acetaminophen has a particle size distribution such that about 90% wt. is below 150 microns and about 35% wt. is below about 40 microns.

20. The acetaminophen composition of claim 16 wherein the amount of solubilized acetaminophen is below 0.95% wt.

21. A method for preparing a taste-masked acetaminophen composition having from about 0.03 to about 0.3% by weight suspension agent and at least 25 weight percent sweetening agent, comprising:

(a) providing an aqueous medium comprising said suspension agent and said sweetening agent; and

(b) admixing particulate acetaminophen to the aqueous medium.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US94/07037

A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) :A61K 31/165
US CL :514/629, 974

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/629, 974

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US, A, 3,142,621 (LAZARUS ET AL) 28 JULY 1964, column 1, lines 31, 34; column 4, example 4; column 5, example 6.	1-21
Y	US, A, 3,317,377 (HILL ET AL) 02 MAY 1967, see column 2, example 1.	1-21
X, P	US, A, 5,272,137 (BLASE ET AL) 21 DECEMBER 1993, column 8, example 1 and column 9, example 2.	1-5, 10, 13

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
09 SEPTEMBER 1994	21 SEP 1994
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer WILLIAM JARVIS Telephone No. (703) 308-1235

Form PCT/ISA/210 (second sheet)(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US94/07037

B. FIELDS SEARCHED
Electronic data bases consulted (Name of data base and where practicable terms used):

APS
search terms: taste, mask, hide, conceal, acetaminophen, sucrose, glucose, fructose, lactose, maltose, sorbitol, mannitol, maltilol, xanthan gum, alginate, carrageenan, carboxymethylcellulose, guar gum, propylene glycol, glycerin, polyethylene glycol